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Atherosclerotic renovascular disease in the United States

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Atherosclerotic renovascular disease (ARVD) is an increasingly recognized clinical condition that is diagnosed predominantly in older patients. Here we used annual United States Medicare 5% Denominator Files and studied 16,036,904 patients, 66 years of age and older, to quantify trends in diagnostic rates, associations, treatment, and outcomes of ARVD over a 13-year period. Overall, there was an ARVD rate of 3.09 per 1000 patient-years, which rose progressively with an adjusted hazard ratio of 3.35, comparing data from 1992 to 2004. Within 6 months of disease diagnosis, 13.4% of patients had undergone revascularization. A biphasic pattern of revascularization was found where the adjusted hazard ratios significantly increased in a progressive manner until 1999, following which there was a decline through 2004, which was not significant. The method of revascularization changed markedly over time with endovascular intervention steadily replacing direct surgical revascularization. As a time-dependent variable, ARVD was associated with excess mortality in each calendar year, albeit with declining hazard ratio estimates in more recent years. Among patients with this disease, revascularization was associated with mortality adjusted hazard ratios <1 in each year. Our study shows the diagnosis of ARVD has substantially risen in the United States but the survival implications were not fully explained by other comorbid vascular diseases.

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Atherosclerotic renovascular disease (ARVD), an increasingly recognized clinical condition, is diagnosed predominantly in older populations.[1] It is believed to be more prevalent in populations with hypertension, chronic kidney disease, atherosclerotic heart disease, congestive cardiac failure, peripheral vascular disease, and cerebrovascular disease,[2–9] and these associations may be partly responsible for high mortality rates associated with ARVD.[10] Strategies with the potential to alter the natural history of this condition are currently being evaluated. Although clinical impression suggests that the burden of ARVD is increasing, and ARVD prevalence has risen considerably in patients starting renal replacement therapy,[11] few, if any, studies have attempted to systematically address this hypothesis in general population settings. The purpose of this study, therefore, was to quantify trends in the diagnosis rates, associations, treatment, and outcomes of ARVD in older US adults between 1992 and 2004.

RESULTS

Of the 16,036,904 study subjects, 48.9% were aged <75 years, 60.2% were women, and 88.6% were white (Table 1). Over the course of the study, incidence of ARVD diagnosis was 3.09 per 1000 patient-years. Regarding sources of Medicare claim ascertainment for ARVD diagnosis, the proportions from Part A (covering in-patient care in hospitals, skilled nursing facilities, hospice, and home health care) alone, for each year from 1992 to 2004, respectively, were 31.45, 28.65, 25.33, 25.01, 24.32, 26.00, 25.07, 24.41, 24.28, 23.12, 20.44, 18.67, and 19.41; corresponding proportions from Part B (covering outpatient care, physician services, physical therapy, occupational therapy, and home health care) alone were 43.65, 50.03, 49.63, 47.72, 47.56, 44.72, 44.49, 43.64, 44.46, 45.51, 46.64, 48.20, and 49.06; and from Part A and Part B together, 24.90, 21.32, 25.04, 27.27, 28.12, 29.28, 30.43, 31.94, 31.26, 31.37, 32.92, 33.12, and 31.53. Hazard ratios for ARVD diagnosis rose progressively by calendar year (Figure 1). For example, with 1992 as reference category, unadjusted hazard ratios were 2.15 for 1997 and 4.71 for 2004. Findings were similar when adjustment was made for baseline characteristics (Table 1), except for moderate attenuation of hazard ratio estimates.

Table 1 | Baseline characteristics, 1992–2004 (*n*=16,036,904), and associations with future diagnosis of atherosclerotic renovascular disease[a]

Characteristic	Percentage	Reference category	Hazard ratio for ARVD (95% CI) Unadjusted	*P*-value	Adjusted	*P*-value
Cohort year		1992				
1992	8.07		1	—	1	—
1993	8.01		1.29 (1.20–1.38)	<0.0001	1.26 (1.17–1.35)	<0.0001
1994	8.10		1.41 (1.32–1.51)	<0.0001	1.33 (1.25–1.43)	<0.0001
1995	7.95		1.77 (1.65–1.88)	<0.0001	1.62 (1.52–1.73)	<0.0001
1996	7.72		1.91 (1.79–2.03)	<0.0001	1.69 (1.58–1.80)	<0.0001
1997	7.50		2.15 (2.01–2.29)	<0.0001	1.85 (1.74–1.97)	<0.0001
1998	7.30		2.44 (2.29–2.60)	<0.0001	2.06 (1.94–2.19)	<0.0001
1999	7.24		2.82 (2.66–3.00)	<0.0001	2.33 (2.20–2.48)	<0.0001
2000	7.27		3.21 (3.02–3.40)	<0.0001	2.58 (2.43–2.74)	<0.0001
2001	7.48		3.79 (3.58–4.02)	<0.0001	2.94 (2.77–3.12)	<0.0001
2002	7.70		4.07 (3.84–4.31)	<0.0001	3.07 (2.89–3.25)	<0.0001
2003	7.82		4.69 (4.43–4.97)	<0.0001	3.44 (3.25–3.64)	<0.0001
2004	7.85		4.71 (4.45–4.99)	<0.0001	3.35 (3.17–3.55)	<0.0001
Age, years		66–74				
66–74	48.89		1	—	1	—
75–84	37.70		1.32 (1.30–1.35)	<0.0001	1.05 (1.03–1.07)	<0.0001
⩾85	13.41		0.91 (0.88–0.94)	<0.0001	0.65 (0.63–0.67)	<0.0001
Sex		Men				
Men	39.82	Women	1	—	1	
Women	60.18		0.82 (0.80–0.83)	<0.0001	0.87 (0.85–0.89)	<0.0001
Race		White				
White	88.62		1	—	1	—
African American	7.44		0.96 (0.93–1.00)	0.03	0.81 (0.78–0.84)	<0.0001
Other	3.94		0.79 (0.75–0.84)	<0.0001	0.71 (0.68–0.75)	<0.0001
Acute kidney injury	0.55	Absent	5.90 (5.57–6.24)	<0.0001	1.05 (0.99–1.12)	0.1
CKD	1.56	Absent	6.61 (6.40–6.82)	<0.0001	2.55 (2.46–2.65)	<0.0001
Diabetes mellitus	15.05	Absent	2.33 (2.28–2.37)	<0.0001	1.31 (1.28–1.33)	<0.0001
Hypertension	41.10	Absent	3.37 (3.31–3.44)	<0.0001	2.20 (2.15–2.25)	<0.0001
ASHD	17.92	Absent	3.04 (2.99–3.10)	<0.0001	1.76 (1.72–1.79)	<0.0001
CHF	9.15	Absent	2.53 (2.47–2.59)	<0.0001	1.10 (1.07–1.14)	<0.0001
Cerebrovascular disease	7.46	Absent	2.49 (2.43–2.56)	<0.0001	1.31 (1.28–1.35)	<0.0001
Dysrhythmia	12.62	Absent	2.08 (2.04–2.13)	<0.0001	1.03 (1.01–1.06)	0.01
PVD	8.17	Absent	3.50 (3.43–3.58)	<0.0001	2.06 (2.01–2.11)	<0.0001
COPD	10.46	Absent	1.75 (1.71–1.79)	<0.0001	1.03 (1.01–1.06)	0.01
GI bleeding	3.29	Absent	1.74 (1.67–1.81)	<0.0001	0.97 (0.93–1.01)	0.1
Hepatic disease	0.52	Absent	1.54 (1.39–1.71)	<0.0001	0.89 (0.80–0.98)	0.02
Malignancy	8.65	Absent	1.26 (1.23–1.30)	<0.0001	0.99 (0.96–1.02)	0.3
Anemia	9.76	Absent	2.15 (2.10–2.20)	<0.0001	1.01 (1.07–1.13)	<0.0001
Mesenteric ischemia	0.13	Absent	2.41 (2.04–2.84)	<0.0001	1.07 (0.90–1.26)	0.5
Aortic aneurysm	0.25	Absent	3.67 (3.33–4.04)	<0.0001	1.28 (1.16–1.41)	<0.0001

ARVD, atherosclerotic renovascular disease; ASHD, atherosclerotic heart disease; CHF, congestive heart failure; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease, GI, gastrointestinal; PVD, peripheral vascular disease.
[a]All subjects were included. Cox regression was used to calculate hazard ratios for future diagnosis of ARVD. Adjustment was made for all variables shown in the first column.

Other characteristics associated with adjusted hazard ratios (AHRs) >1.20 included chronic kidney disease (AHR 2.55), hypertension (AHR 2.20), peripheral vascular disease (AHR 2.06), atherosclerotic heart disease (AHR 1.76), cerebrovascular disease (AHR 1.31), diabetes mellitus (AHR 1.31), and aortic aneurysm (AHR 1.28); AHR was <0.83 for age ⩾85 (AHR 0.65), other race (AHR 0.71), and African-American race (AHR 0.81).

Of the 47,719 patients diagnosed with ARVD, 6415 (13.4%) underwent revascularization within 6 months of receiving the diagnosis. Compared with 1992, unadjusted hazard ratios for revascularization rose progressively by calendar year until 1999, thereafter declining progressively until 2004 (Figure 2). Mean ages of patients with ARVD, for each year from 1992 through 2004, respectively, were 74.79, 75.07, 75.09, 75.31, 75.63, 75.77, 75.84, 75.92, 76.10, 76.22, 76.32, 76.37, and 76.51 years. Findings were similar when adjustment was made for baseline characteristics (Table 2), except for moderate attenuation of hazard ratio estimates. Characteristics associated with AHR >1.20 for revascularization included hypertension (AHR 1.37) and atherosclerotic heart disease (AHR 1.27); AHR was <0.83 for age ⩾85 (AHR 0.47), hepatic disease (AHR 0.69), African-American race (AHR 0.71), other race (AHR 0.73), and malignancy (AHR 0.82). The pattern of revascularization technique changed markedly over time (Table 3), with endovascular

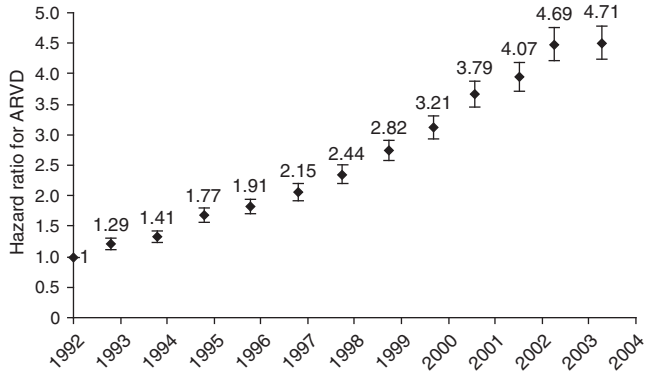

Figure 1 | Unadjusted hazard ratios, with 95% confidence intervals, for atherosclerotic renovascular disease (ARVD) by calendar year, with 1992 as reference category.

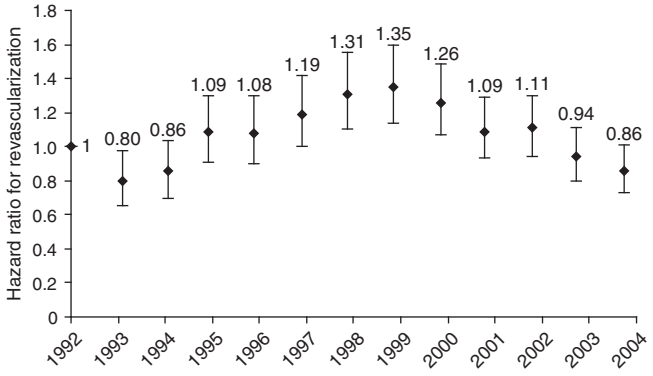

Figure 2 | Subjects diagnosed with atherosclerotic renovascular disease: unadjusted hazard ratios, with 95% confidence intervals, for revascularization within the ensuing 6 months by calendar year, with 1992 as reference category. $P<0.05$; 1993, $P=0.03$; 1998, $P=0.002$; 1999, $P=0.0004$; 2000, $P=0.006$.

intervention (67.4% in 1992, 98.5% in 2004) steadily replacing direct surgical revascularization. Surgical revascularization was used for only 2.1% of revascularized patients in 2004. Among patients undergoing percutaneous revascularization, the proportions who received stents, for each year from 1992 through 2004, respectively, were 13.33, 27.27, 35.80, 48.11, 57.68, 63.01, 71.15, 71.96, 69.08, 69.73, 63.61, 68.51, and 67.61; corresponding proportions of patients who did not receive stents were 86.67, 72.23, 64.20, 51.89, 42.32, 36.99, 28.85, 28.04, 30.92, 30.27, 36.39, 31.49, and 32.39.

Over a mean follow-up interval of 2.68 years, 2,487,580 study subjects (15.51%) died, a rate of 57.87 per 1000 patient-years. Figure 3 shows year-by-year trends in adjusted mortality ratios for ARVD as a conditional event in the overall study population, and for revascularization as a conditional event in patients with ARVD. ARVD was associated with excess mortality compared with the general population in each calendar year, albeit with apparent declines in hazard ratio estimates in more recent years. Hazard ratios for mortality in ARVD patients undergoing revascularization were <1 in each year; moderate year-to-year variation was apparent, but there was no clear evidence that hazard ratios had changed over time.

DISCUSSION

We observed a steady increase in ARVD diagnoses in US patients aged >65 years, with likelihood of the diagnosis 3 times greater in 2002 than when the study began in 1992. As this was a nonexperimental study based on administrative claims, the relative contribution of increasing disease burden and increased detection rates at earlier disease phases is impossible to gauge. This being said, it is highly likely that diagnostic modalities for ARVD improved between 1992 and 2004, with techniques such as ultrasound, computed tomography, and magnetic resonance imaging facilitating noninvasive ARVD detection. Related to this, the study era prevented us from assessing whether rates of ARVD diagnosis have declined as a result of concern about gadolinium-associated nephrogenic systemic fibrosis with magnetic resonance imaging angiography.[12,13] The associations of ARVD with other major macrovascular pathologies, chronic kidney disease, hypertension, and diabetes have been well-described in recent large epidemiologic studies.[10,11] As noted in these studies, patients aged >85 years and those of races other than white were less likely to be diagnosed with ARVD. Even with extensive covariate adjustment in our study, individuals of race or ethnicity other than white were less likely to be diagnosed with ARVD, and, if they were diagnosed, less likely to undergo revascularization. Although a firm explanation cannot be established from our study, this disparity suggests the possibility of nonmedical barriers to appropriate investigation and care.

In the mid-to-late 1990s, use of renal revascularization to treat ARVD increased, possibly coinciding with widespread adoption of percutaneous renal angioplasty techniques.[14] However, it was interesting to note the steady decline in proportions of patients undergoing revascularization procedures after 1999. This decline may reflect growing uncertainty regarding appropriate management of ARVD, particularly considering the lack of robust clinical trial evidence to guide clinical practice.[15] For example, we found that, among patients diagnosed with ARVD, revascularization was more likely from 1997 through 2000, with the return to pre-1997 levels from 2001 to 2004. Interestingly, two landmark studies were published in 1997 and 2000. The former was a prospective study showing favorable outcomes with intravascular stents in patients with critical ostial stenoses,[16] and the latter a randomized, controlled trial showing that percutaneous transluminal renal angioplasty had no long-term effect on blood pressure, antihypertensive medication requirements, or kidney function among patients with ARVD.[17] Possibly, ARVD diagnoses through the 1990s may have included a higher proportion of patients for whom revascularization was considered inappropriate. Without question, however, use of surgical revascularization techniques to treat ARVD markedly decreased year on year throughout the decade of the study, so that by 2004 more than 97% of renal artery revascularization procedures were performed percutaneously. This phenomenon, which has been described previously among Medicare beneficiaries

Table 2 | Patients diagnosed with atherosclerotic renovascular disease: antecedent associations of revascularization[a]

Characteristic	Reference category	Hazard ratio for revascularization for ARVD (95% CI)			
		Unadjusted	*P*-value	Adjusted	*P*-value
Cohort year	1992				
1992		1	—	1	—
1993		0.80 (0.65–0.98)	0.03	0.82 (0.66–1.00)	0.05
1994		0.86 (0.70–1.04)	0.1	0.87 (0.72–1.06)	0.2
1995		1.09 (0.91–1.30)	0.4	1.10 (0.91–1.32)	0.3
1996		1.08 (0.90–1.30)	0.4	1.09 (0.91–1.31)	0.3
1997		1.19 (1.00–1.42)	0.05	1.20 (1.01–1.43)	0.04
1998		1.31 (1.10–1.55)	0.002	1.32 (1.11–1.56)	0.002
1999		1.35 (1.14–1.60)	0.0004	1.35 (1.14–1.60)	0.0004
2000		1.26 (1.07–1.49)	0.006	1.27 (1.07–1.50)	0.005
2001		1.09 (0.93–1.29)	0.3	1.10 (0.93–1.29)	0.3
2002		1.11 (0.94–1.30)	0.2	1.11 (0.95–1.31)	0.2
2003		0.94 (0.80–1.11)	0.4	0.94 (0.80–1.11)	0.5
2004		0.86 (0.73–1.01)	0.06	0.86 (0.73–1.02)	0.08
Age, years	66–74				
66–74		1	—	1	—
75–84		0.92 (0.87–0.96)	0.0007	0.90 (0.86–0.95)	<0.0001
⩾85		0.47 (0.42–0.53)	<0.0001	0.47 (0.42–0.53)	<0.0001
Sex	Men				
Men	Women	1	—	1	—
Women		1.04 (0.99–1.09)	0.1	1.06 (1.00–1.11)	0.04
Race	White				
White		1	—	1	—
African American		0.72 (0.65–0.81)	<0.0001	0.71 (0.64–0.79)	<0.0001
Other		0.73 (0.63–0.86)	0.0001	0.73 (0.62–0.86)	0.0001
Acute kidney injury	Absent	0.98 (0.83–1.14)	0.8	1.07 (0.91–1.27)	0.4
CKD	Absent	0.95 (0.87–1.04)	0.3	0.97 (0.88–1.07)	0.5
Diabetes mellitus	Absent	0.98 (0.93–1.04)	0.5	0.93 (0.88–0.98)	0.009
Hypertension	Absent	1.34 (1.27–1.42)	<0.0001	1.37 (1.29–1.45)	<0.0001
ASHD	Absent	1.23 (1.17–1.29)	<0.0001	1.27 (1.20–1.34)	<0.0001
CHF	Absent	0.95 (0.89–1.02)	0.1	0.96 (0.89–1.03)	0.3
Cerebrovascular disease	Absent	1.18 (1.11–1.26)	<0.0001	1.14 (1.07–1.22)	0.0001
Dysrhythmia	Absent	0.92 (0.87–0.98)	0.01	0.89 (0.84–0.95)	0.0005
PVD	Absent	1.03 (0.97–1.09)	0.4	0.99 (0.93–1.05)	0.7
COPD	Absent	0.92 (0.86–0.99)	0.02	0.89 (0.83–0.96)	0.001
GI bleeding	Absent	0.93 (0.83–1.04)	0.2	0.98 (0.87–1.10)	0.8
Hepatic disease	Absent	0.67 (0.48–0.95)	0.03	0.69 (0.48–0.97)	0.04
Malignancy	Absent	0.80 (0.73–0.87)	<0.0001	0.82 (0.75–0.90)	<0.0001
Anemia	Absent	0.85 (0.79–0.90)	<0.0001	0.85 (0.79–0.92)	<0.0001
Mesenteric ischemia	Absent	0.79 (0.48–1.32)	0.4	0.76 (0.46–1.26)	0.3
Aortic aneurysm	Absent	0.92 (0.70–1.20)	0.5	0.87 (0.66–1.15)	0.3

ARVD, atherosclerotic renovascular disease; ASHD, atherosclerotic heart disease; CI, confidence interval; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease, GI, gastrointestinal; PVD, peripheral vascular disease.
[a]Analysis restricted to patients diagnosed with atherosclerotic renovascular disease. Cox regression was used to calculate hazard ratios for revascularization. Adjustment was made for all variables shown in the first column.

Table 3 | Mode of revascularization for atherosclerotic renovascular disease by calendar year, with 1992 as reference category

Cohort year	*n*	Angioplasty/stent only, %	Surgery only, %	Angioplasty/stent and surgery, %	*P*-value (vs 1992)
1992	178	64.61	32.58	2.81	—
1993	183	69.95	27.87	2.19	0.6
1994	217	72.35	25.35	2.30	0.3
1995	332	77.11	20.48	2.41	0.009
1996	347	83.00	15.56	1.44	<0.0001
1997	417	85.37	12.47	2.16	<0.0001
1998	508	89.57	7.87	2.56	<0.0001
1999	604	92.22	6.13	1.66	<0.0001
2000	650	95.08	4.46	0.46	<0.0001
2001	698	95.42	3.44	1.15	<0.0001
2002	781	97.18	2.18	0.64	<0.0001
2003	782	96.55	2.94	0.51	<0.0001
2004	718	97.91	1.53	0.56	<0.0001

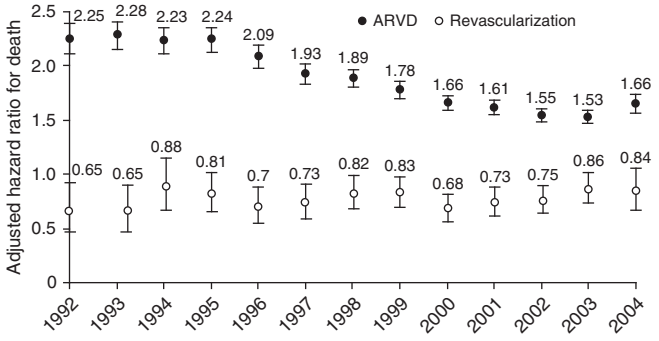

Figure 3 | Closed circles represent adjusted mortality hazard ratios, with 95% confidence intervals, of atherosclerotic renovascular disease (ARVD) in the overall population by calendar year, with ARVD treated as a conditional, time-dependent event. $P<0.0001$ for each calendar year. Open circles represent mortality hazard ratios of ARVD revascularization in subjects with ARVD by calendar year. Subjects diagnosed with ARVD (open circles): adjusted, with ARVD revascularization treated as a conditional, time-dependent event. Adjustment was made for all the characteristics shown in the first column of Table 1. $P<0.05$; 1992, $P=0.01$; 1993, $P=0.01$; 1996, $P=0.002$; 1997, $P=0.005$; 1998, $P=0.04$; 1999, $P=0.03$; 2000, $P<0.0001$; 2001, $P=0.0006$; 2002, $P=0.0009$.

between 1996 and 2000,[18] likely reflects the fact that technical outcomes are usually excellent with percutaneous approaches, and procedure-related morbidity, mortality, and hospitalization requirements may be lower than with surgical intervention. Although mortality risk was higher for ARVD patients than for the general Medicare population for each cohort year, the adjusted risk progressively declined over time, perhaps implying that earlier recognition (one major explanation for the trend in increasing ARVD diagnoses) enabled earlier and more effective vascular disease management. Revascularization was associated with improved mortality risk in each ARVD cohort year, but the influence of selection factors on this treatment effect cannot be ascertained in this study.

Results of large, multicenter, randomized international trials, designed to establish whether renal revascularization can improve the major outcomes of renal functional stability and patient mortality, are likely to influence the approach to revascularization in the future. One recently published multicenter, randomized, clinical trial compared the effect of stent placement on renal function in patients with creatinine clearance less than 80 ml/min per 1.73 m^2 and atherosclerotic renal artery stenosis of $>50\%$ who were already receiving antihypertensive, statin, and aspirin therapy. Stent placement had no effect on the evolution of renal dysfunction. The authors suggest that a conservative medical approach might be appropriate for most patients with ARVD, given that stenting was occasionally followed by serious clinical complications such as procedure-related death, infected hematoma, and end-stage renal disease from cholesterol embolism.[19] Initial data reported from the Angioplasty and STent for Renal Artery Lesions (ASTRAL) trial,[20] with more than 800 patients followed for a mean period of 34 months, suggest that renal endovascular revascularization with medical therapy provides no clinically important benefit for renal function (the primary end point), blood pressure, cardiac and renal events, or mortality, compared with medical therapy alone. The Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) study[21] has a different primary end point (a composite cardiovascular and renal end point: cardiovascular or renal death, myocardial infarction, hospitalization for congestive heart failure, stroke, doubling of serum creatinine, and need for renal replacement therapy), and is still recruiting patients.

Limitations of this study are that it was retrospective and used administrative claims to define the study population and outcomes. The accuracy of ARVD claims for ARVD diagnosis could not be ascertained in this study. Conceivably, ARVD may often have been an incidental finding during the diagnostic work-up of patients with disease in nonrenal vascular beds. The Medicare patient random samples that we studied included older US populations, and caution should be exercised in generalizing our findings to younger populations or to other countries.

We believe that this study provides clinically important information, particularly in relation to the evolution of trends in clinician practice with respect to investigation and management of this common condition. Notably, awareness of increasing ARVD diagnoses, and of trends in use of revascularization procedures, will be of interest to health-care service providers. Results of the large international trials in renovascular disease will further shape the epidemiology and management of the condition in the future.

MATERIAL AND METHODS

Objectives

Among US adults aged $\geqslant 66$ years, we set out to quantify the following:

1. Trends in diagnosis rates of ARVD from 1992 through 2004, the primary objective.
2. Antecedent associations of ARVD.
3. Trends in revascularization for ARVD from 1992 through 2004.
4. Associations of revascularization for ARVD.

Patients and outcomes

In the United States, Medicare insurance coverage is universally available from age 65 years. We used the United States Medicare 5% Denominator File,[22,23] a random sample based on health insurance claim numbers. Major design features are shown in Figure 4. Study subjects had the following characteristics: continuous enrollment in Medicare Part A and Part B from 1 January through 31 December of each study year, 1992 to 2004; survival to 31 December of each calendar year; aged $\geqslant 66$ years on 31 December of each calendar year. Patients enrolled in health maintenance organizations, with Medicare as secondary payer; diagnosed with ARVD or end-stage renal disease during the exposure period; or not residing in the 50 US states, the District of Columbia, Puerto Rico, or the Territories during each year were excluded.

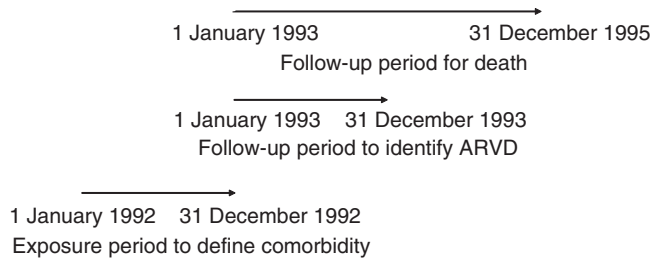

Figure 4 | Definition of exposure and follow-up periods for 1992. ARVD, atherosclerotic renovascular disease.

Baseline clinical characteristics were defined during the 1-year exposure periods using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Current Procedural Terminology (CPT) codes, as shown in the Appendix; codes for ARVD and renal revascularization occurrence during the observation period are also shown. ARVD and renal revascularization were defined by presence of at least one ICD-9-CM or CPT procedural code. The specific codes used to identify ARVD were 440.1 (atherosclerosis of renal artery) and 593.81 (vascular disorders of kidney). Other clinical conditions were defined by presence of one in-patient hospitalization, skilled nursing facility, or home health agency code, or two outpatient or physician/supplier codes less than 1 year apart, or one outpatient code and one physician/supplier code less than 1 year apart.

Analysis

For ARVD ascertainment, patients in each annual cohort were followed from 1 January of the succeeding year until the earliest occurrence of ARVD diagnosis, death, renal replacement therapy, change of health insurance payer status, or 31 December. For example, for the 1992 cohort, ARVD occurrence was defined by an appropriate ICD-9-CM or CPT code between 1 January 1992, and 31 December 1993. For renal revascularization, follow-up began at the first occurrence of ARVD and ended at the earliest occurrence of an appropriate ICD-9-CM or CPT claim, death, renal replacement therapy, change of health insurance payer status, or 6 months. For mortality events, patients were followed until the earliest occurrence of death, renal replacement therapy, 3 years, or 31 December 2006. Cox proportional hazard modeling was used to quantify hazard ratios of baseline population characteristics for time to ARVD occurrence and revascularization after ARVD. As ARVD and revascularization are conditional events that may not necessarily occur during the follow-up period, these were treated as time-dependent variables in Cox time-to-death models. SAS Version 9.1 (SAS Institute, Cary, NC) was used for data assembly.

DISCLOSURE

The authors declared no competing of interests.

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REFERENCES

1. Hansen KJ, Edwards MS, Craven TE *et al.* Prevalence of renovascular disease in the elderly: a population-based study. *J Vasc Surg* 2002; **36**: 443–451.
2. Harding MB, Smith LR, Himmelstein SI *et al.* Renal artery stenosis: prevalence and associated risk factors in patients undergoing routine cardiac catheterization. *J Am Soc Nephrol* 1992; **2**: 1608–1616.
3. Crowley JJ, Santos RM, Peter RH *et al.* Progression of renal artery stenosis in patients undergoing cardiac catheterization. *Am Heart J* 1998; **136**: 913–918.
4. MacDowall P, Kalra PA, O'Donoghue DJ *et al.* Risk of morbidity from renovascular disease in elderly patients with congestive cardiac failure. *Lancet* 1998; **352**: 13–16.
5. Choudhri AH, Cleland JG, Rowlands PC *et al.* Unsuspected renal artery stenosis in peripheral vascular disease. *Br Med J* 1990; **301**: 1197–1198.
6. Olin JW, Melia M, Young JR *et al.* Prevalence of atherosclerotic renal artery stenosis in patients with atherosclerosis elsewhere. *Am J Med* 1990; **88**: 46N–51N.
7. Kuroda S, Nishida N, Uzu T *et al.* Prevalence of renal artery stenosis in autopsy patients with stroke. *Stroke* 2000; **31**: 61–65.
8. Shurrab AE, MacDowall P, Wright J *et al.* The importance of associated extra-renal vascular disease on the outcome of patients with atherosclerotic renovascular disease. *Nephron Clin Pract* 2003; **93**: C51–C57.
9. Cheung CM, Hegarty J, Kalra PA. Dilemmas in the management of renal artery stenosis. *Br Med Bull* 2005; **73-74**: 35–55.
10. Kalra PA, Guo H, Kausz AT *et al.* Atherosclerotic renovascular disease in United States patients aged 67 years or older: risk factors, revascularization, and prognosis. *Kidney Int* 2005; **68**: 293–301.
11. Guo H, Kalra PA, Gilbertson DT *et al.* Atherosclerotic renovascular disease in older US patients starting dialysis, 1996 to 2001. *Circulation* 2007; **115**: 50–58.
12. Marckmann P, Skov L, Rossen K *et al.* Nephrogenic systemic fibrosis: suspected causative role of gadodiamide used for contrast-enhanced magnetic resonance imaging. *J Am Soc Nephrol* 2006; **17**: 2359–2362.
13. Sadowski EA, Bennett LK, Chan MR *et al.* Nephrogenic systemic fibrosis: risk factors and incidence estimation. *Radiology* 2007; **243**: 148–157.
14. Bonelli FS, McKusick MA, Textor SC *et al.* Renal artery angioplasty: technical results and clinical outcome in 320 patients. *Mayo Clin Proc* 1995; **70**: 1041–1052.
15. Nordmann AJ, Hengstler P, Leimenstoll BM *et al.* Clinical outcomes of stents versus balloon angioplasty in non-acute coronary artery disease. A meta-analysis of randomized controlled trials. *Eur Heart J* 2004; **25**: 69–80.
16. Blum U, Krumme B, Flugel P *et al.* Treatment of ostial renal-artery stenoses with vascular endoprostheses after unsuccessful balloon angioplasty. *N Engl J Med* 1997; **336**: 459–465.
17. van Jaarsveld BC, Krijnen P, Pieterman H *et al.* The effect of balloon angioplasty on hypertension in atherosclerotic renal-artery stenosis. Dutch Renal Artery Stenosis Intervention Cooperative Study Group. *N Engl J Med* 2000; **342**: 1007–1014.
18. Murphy TP, Soares G, Kim M. Increase in utilization of percutaneous renal artery interventions by medicare beneficiaries, 1996–2000. *AJR Am J Roentgenol* 2004; **183**: 561–568.
19. Bax L, Woittiez AJ, Kouwenberg HJ *et al.* Stent placement in patients with atherosclerotic renal artery stenosis and impaired renal function: a randomized trial. *Ann Intern Med* 2009; **150**: 840–841.
20. Wheatley K, Kalra PA, Moss J *et al.* Lack of benefit of renal artery revascularization in atherosclerotic renovascular disease (ARVD): results of the ASTRAL trial. *J Am Soc Nephrol* 2008; **19**: 7A. (abstract F-FC206).
21. Cooper CJ, Murphy TP, Matsumoto A *et al.* Stent revascularization for the prevention of cardiovascular and renal events among patients with renal artery stenosis and systolic hypertension: rationale and design of the CORAL trial. *Am Heart J* 2006; **152**: 59–66.
22. Research Data Assistance Center. Medicare Data File Descriptions. Available at: http://www.resdac.umn.edu/Medicare/data_file_descriptions.asp Accessed July 31 2009.
23. Research Data Assistance Center. Differences in How the Medicare 5% Files are Generated. March 2007. Available at: http://www.resdac.umn.edu/Tools/TBs/TN-011_How5percentMedicarefilescreated_508.pdf Accessed July 31 2009.

Appendix

International classification of diseases, ninth edition, clinical modification and current procedural terminology codes

	International classification of diseases, ninth edition, clinical modification			
Condition	Diagnosis codes	V codes	Procedure codes	Current procedural terminology codes
ASHD	410–414	V45.81; V45.82		
CHF	398.91; 425; 428; 402.X1; 404.x1; 404.x3	V42.1		
CVA/TIA	430–438			
PVD	440–444, except for 4401 and 4400; 447; 451–453			
COPD	491–494; 496; 510			
GI disease	456.0–456.2; 530.7; 531–534; 569.84; 569.85; 578			
Liver disease	570; 571; 572.1; 572.4; 573.1–573.3	V42.7		
Dysrhythmia	426–427	V45.0, V53.3		
Diabetes mellitus	250; 357.2; 362.0x; 366.41			
Cancer	140–172; 174–208; 230–231; 233–234			
Anemia	280–285			
CKD	250.4; 403.X1; 404.X2; 404.X3; 585–587; 794.4			
Hypertension	362.11; 401.x–405.x; 437.2			
AKD	584.x			
Gut ischemia	557.0; 557.1; 557.9			
Aortic aneurysm	440.0		39.71; 38.36; 38.44; 38.16	
ARVD	440.1; 593.81			
Renal Revascularization			39.24; 38.10, 39.29, 39.50 2 weeks before or after 88.45	35536 35636; 35560; 35450, 35471, 35631, 75966 with no prior 75726; 37205, 37206, 37207, 37208 with no prior 75726 and with 35450, 35471, or 75966 4 weeks prior

AKD, acute kidney disease; ARVD, atherosclerotic renovascular disease; ASHD, atherosclerotic heart disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA/TIA, cerebrovascular accident or transient ischemic attack; GI, gastrointestinal; PVD; peripheral vascular disease.